NOVEL FORMULATIONS FOR OPIOID-BASED TREATMENTS OF PAIN COMPRISING 1-(1,2-DISUBSTITUTED PIPERIDINYL)-4-SUBSTITUTED PIPERAZINE DERIVATIVES

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This invention concerns novel formulations for opioid-based treatments of pain and/or nociception comprising opioid analgesics and 1-(1,2-disubstituted piperidinyl)-4-substituted piperazine derivatives having neurokinin antagonistic activity, in particular NK₁ antagonistic activity the use of said formulation for the manufacture of a medicament for the prevention and/or treatment of emesis, pain and/or nociception, in particular in acute and chronic pain treatments, more in particular in inflammatory, post-operative, emergency room (ER), breakthrough, neuropathic and cancer pain treatments and the use of an NK₁-receptor antagonist for the manufacture of a medicament for the prevention and/or treatment of respiratory depression and tolerance in opioid-based treatments of pain.

The pharmaceutical formulations according to the invention comprise NK₁-antagonists according to the general Formula (I)

$$\begin{array}{c|c}
 & R^{1} \\
 & \downarrow \\
 & R^{2} - X
\end{array}$$

$$\begin{array}{c|c}
 & R^{1} \\
 & \downarrow \\
 & (CH_{2})_{m} \\
 & (CH_{2})_{n}
\end{array}$$

$$\begin{array}{c|c}
 & (I) \\
 & (CH_{2})_{p}
\end{array}$$

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the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof and prodrugs thereof, wherein all substituents are defined as in Claim 1.

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The pharmaceutical composition according to the invention reduces to a large extent a number of unwanted side-effects associated with opioid analysesics, in particular respiratory depression and tolerance, thereby increasing the total tolerability of said opioids in pain treatment.